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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/722,176	RANA, TARIQ M.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,19-28,30,33-42 and 45-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,19-28,30,33-42 and 45-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/01/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 10/1/2009 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 04/01/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 08/15/2008, claims 14, 19-28, 30, 33-42 and 45-55 are pending and currently under examination in the application.

New Claim Rejections - 35 USC § 103

The new rejection is necessitated by addition of new claims and claim amendments.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szoka et al. (US Patent No. 5,661,025 of record cited on PTO Form 892 filed

02/26/2008), Tuschl et al. (cited on PTO Form 892 filed 08/23/05) and McManus et al. (cited on PTO Form 892 filed 08/23/05) and Eichman et al. (cited on IDS filed 05/23/2008).

The instant claims are drawn to a delivery mixture comprising a 2 to 5 generation dendrimer mixed with an amount of a nucleic acid effective to mediate RNAi, wherein the delivery mixture can deliver the nucleic acid into the cytoplasm of the cell, wherein the nucleic acid is an RNA molecule, wherein the RNA is a miRNA, a shRNA or a siRNA and wherein the dendrimer is PAMAM.

Szoka et al. teach DNA, RNA and RNA:DNA hybrid oligonucleotide molecules wherein the molecules are mixed with PAMAM dendrimers having generations 2 to 5 (see columns 9 and 10 and see Table 2). Szoka et al. teach the delivery mixture comprising a dendrimer and oligonucleotide is capable of delivering the oligonucleotide molecule to subcellular component of a cell (see column 5). Szoka et al. teach the dendrimer is generally and preferably non-covalently associated with the nucleic acid which permits easy disassociation or disassembling of the dendrimer and nucleic acid once the composition is delivered into the cell (see paragraph 33). Szoka et al. do not teach mixing an amount of nucleic acid effective to mediate RNAi with a dendrimer and do not specifically teach the siRNA.

Tuschl et al. teach siRNA molecules, 19-23 nucleotides in length comprising 3' 2 nucleotide overhangs that are effective at mediating RNAi wherein the nucleotides of the sense strand and antisense strand are complementary to the target gene (see page

6, lines 8-15 and Figure 14). Likewise, McManus et al. teach shRNA and microRNA which are effective at mediating RNAi (see page 740).

Eichman et al. teach the mechanism of dendrimer-mediated cell entry. Eichman et al. teach on pages 236-237 and Figure 7 that the dendrimer complexed with nucleic acid is delivered to the cytoplasm of the cell by cell surface attachment and endocytosis where there is endosomal release and the nucleic acid is dissociated from the dendrimer. Eichman et al. teach that the nucleic acid is then translocated to the nucleus alone or in some cases can be still attached to the dendrimer. Eichman et al. teach the dendrimer complex allowed for more efficient delivery of nucleic acids into the cell without causing cytotoxicity or nucleic acid degradation (see at least page 239 and conclusion)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the delivery mixture comprising a dendrimer as taught by Szoka et al. for delivering a siRNA, microRNA or shRNA as taught by Tuschl et al. and McManus et al.

One would have been motivated to make a delivery mixture comprising a dendrimer and a siRNA or a microRNA or shRNA because Tuschl et al. and McManus et al. both teach such nucleic acid compounds are more efficient at silencing gene expression and are very useful for determining the function of a gene. In probing gene function and inhibition of gene expression, one of skill in the art would be motivated to use the most efficient methodology for mediating RNAi efficiently in cells, thereby allowing elucidation of gene function. Because siRNA is an inhibitory nucleic acid

molecule, one would expect to encounter similar issues in delivery to cells as with the previously known oligonucleotides and therefore one would be motivated to use a delivery mixture comprising a dendrimer because the goal for RNAi is optimal delivery of the siRNA and enhanced cellular uptake by the cells.

The use of dendrimers in a delivery mixture, as claimed by the instant invention, were known to add benefits to delivery of oligonucleotides molecules to cells and therefore one would have been motivated to make a delivery mixture comprising siRNA and test various ranges for the optimal concentration.

Applicant's arguments regarding the unobviousness of combining a siRNA with a dendrimer complex will be addressed since it would apply to the new rejection above. Applicant argues Szoka et al. teach the dendrimer plus oligonucleotide mixture delivery the antisense oligonucleotides to the nucleus and because it is known that RNAi is mediated by the interaction of siRNA with cytoplasmic RISC complex it would not be easy to predict whether a delivery mixture of dendrimer and siRNA would be delivered to the nucleus or the cytoplasm and whether RNAi would result. This argument is not persuasive because first, the claims are not drawn to any limitation that requires the nucleic acid or siRNA to mediate RNAi in the cytoplasm or that once delivered to the cell the nucleic acid or siRNA must remain in the cytoplasm; the claimed invention only requires the delivery mixture to deliver the nucleic acid to the cytoplasm. However because it was known at the time of the invention that nucleic acids capable of mediating RNAi do associate with the RISC complex in the cytoplasm, all that is

required is for the delivery mixture to deliver the nucleic acid into the cell and dissociate from the dendrimer to be capable of associating with the RISC complex.

Szoka et al. teach the dendrimer is preferably non-covalently associated with the nucleic acid which permits easy disassociation or disassembling of the dendrimer and nucleic acid once the composition is delivered into the cell. Eichman et al. further confirms the mechanism of action of dendrimer mediated delivery of nucleic acid wherein the dendrimer is capable of disassociating from the nucleic acid. While it is true that Eichman et al. teach nucleic acids that enter the nucleus can in fact still be attached to a dendrimer, Eichman et al. nor Szoka et al. teach that the dendrimer can only deliver the nucleic acid to the nucleus. It is clear from the prior art that dendrimers-nucleic acid complexes are capable of efficiently delivering the nucleic acid into the cytoplasm of the cell and therefore depending on the mechanism of action of the nucleic acid, whether it is further translocated into the nucleus to be transcribed or in the case of siRNA associates with RISC, this further processing of the nucleic acid is not a direct action of the dendrimer. This is demonstrated by Applicant's own experiments wherein in paragraph 0111, it is disclosed that dendrimer mixed with siRNA were capable of delivery the siRNA to both cytoplasm and nuclear regions of the cells and therefore any RNAi would be mediated by the siRNA in the cytoplasm.

[0111] The cellular localization with siRNA introduced into cells using a dendrimer was examed. In these experiments, 21-nucleotide 5'-Cy3-labeled sense strand siRNA was deprotected and annealed to unmodified antisense strand and applied to HeLa cells grown to 70% confluency by PAMAM-mediated transfection as described herein. Cells were incubated in 1 mL transfection mixture containing 40 .mu.g PAMAM, 100 pmole 5'Cy3-SS/AS duplex siRNAs for 6 hours at 37.degree. C. and washed three times with PBS (Invitrogen) to remove the transfection mixture. Cells were fixed in 100% methanol (pre-cooled to -20C) for 10 minutes, air dried and then re-hydrated in PBS. The uptake of siRNA in HeLa cells was

monitored by fluorescence microscope using a Cy3 filter. Exemplary data are shown in FIG. 9. Cy3 Fluorescence represents the localization of duplex siRNA (FIGS. 9A, 9D and 9G). **Overlay images of the Cy3 signal (FIGS. 9a, 9d and 9g) with the DIC (FIGS. 9B, 9E and 9H) indicate that PAMAM-mediated delivery can localize siRNA to both cytoplasm and nuclear regions in the cells (FIGS. 9C, 9F and 91).** Much of the Cy3 fluorescence signal was detected in the nuclear region (FIGS. 9C and 9F) indicating that Lipofectamine.TM. and PAMAM-mediated delivery may have different routings. **[emphasis added].**

Thus, one would have a reasonable expectation of success at making a delivery mixture comprising a dendrimer and a siRNA wherein the siRNA would be capable of mediating RNAi given Szoka et al. and Eichman et al. teach the dendrimer mixture is capable of delivering nucleic acids into the cytoplasm.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 112 - maintained

The rejection of claim 14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for the reasons of record.

Applicant's only argument is that they traverse the rejection in view of the amendments to the pending claims. Claim 14 has not been amended and since Applicant's have not provided arguments as to why claim 14 lacks written description, the rejection is maintained.

Re: Claim Rejections - 35 USC § 103 - maintained

The rejection of claims 14, 19-28, 30 and 33-44 under 35 U.S.C. 103(a) as being unpatentable over Szoka et al. (US Patent No. 5,661,025 of record cited on PTO Form 892 filed 02/26/2008), Tuschl et al. (cited on PTO Form 892 filed 08/23/05) and McManus et al. (cited on PTO Form 892 filed 08/23/05) Olejnik et al. (cited on PTO Form 892 filed 08/23/05) and Grigoriev et al. (cited on PTO Form 892 filed 08/23/05) is maintained for the reasons of record.

New claims 45-54 are drawn to the same invention as previous rejected and would have been rejected in the rejection of record and thus the rejection above is maintained for claims 45-54. Response to Applicant's arguments will be addressed with the respect to the new claims.

Applicants arguments are solely drawn to the claimed invention would not have been obvious because the prior art fails to teach delivery of dendrimers and nucleic acids into the cytoplasm of cells and therefore it would not be easy to predict whether a delivery mixture would deliver the nucleic acid to the nucleus or the cytoplasm. It must be pointed out that the claim limitation of delivery to the cytoplasm of cells is only in claims 19 and 55.

Applicant argues it would not be obvious to combine a siRNA with a dendrimer complex and submits Szoka et al. teach the dendrimer plus oligonucleotide mixture is only capable of delivery of antisense oligonucleotides to the nucleus as shown in Examples 23-28 and because it is known that RNAi is mediated by the interaction of siRNA with cytoplasmic RISC complex it would not be easy to predict whether a delivery

mixture of dendrimer and siRNA would be delivered to the nucleus or the cytoplasm and whether RNAi would result.

This argument is not persuasive because first, the claims are not drawn to any limitation that requires the nucleic acid or siRNA to mediate RNAi in the cytoplasm or that once delivered to the cell the nucleic acid or siRNA must remain in the cytoplasm; the claimed invention only requires the delivery mixture to deliver the nucleic acid to the cytoplasm. However because it was known at the time of the invention that nucleic acids capable of mediating RNAi do associate with the RISC complex in the cytoplasm, all that is required is for the delivery mixture to deliver the nucleic acid into the cell and dissociate from the dendrimer to be capable of associating with the RISC complex.

Szoka et al. teach the dendrimer is preferably non-covalently associated with the nucleic acid which permits easy disassociation or disassembling of the dendrimer and nucleic acid once the composition is delivered into the cell (see paragraph 33). Examples 23-28 of Szoka et al. do discuss measuring the amount of oligonucleotide in the nucleus; however these experiments do not disclose that the dendrimer mixture only delivered the oligonucleotide to the nucleus. The Examples disclose attaching a fluorescent molecule to the oligonucleotide and it is this molecule that is measured in the nucleus and not the dendrimer. As pointed to above, Szoka et al. preferably teach the dendrimer is non-covalently associated with the nucleic acid to permit easy disassociation or disassembling of the dendrimer and nucleic acid once the composition is delivered into the cells. Szoka et al. do not teach that the dendrimer can only deliver the nucleic acid to the nucleus. It is clear from the prior art that dendrimers-nucleic acid

complexes are capable of efficiently delivering the nucleic acid into the cytoplasm of the cell and therefore depending on the mechanism of action of the nucleic acid, whether it is further translocated into the nucleus to be transcribed or in the case of siRNA associates with RISC, this further processing of the nucleic acid is not a direct action of the dendrimer. This is demonstrated by Applicant's own experiments wherein in paragraph 0111, it is disclosed that dendrimer mixed with siRNA were capable of delivery the siRNA to both cytoplasm and nuclear regions of the cells and therefore any RNAi would be mediated by the siRNA in the cytoplasm.

[0111] The cellular localization with siRNA introduced into cells using a dendrimer was examed. In these experiments, 21-nucleotide 5'-Cy3-labeled sense strand siRNA was deprotected and annealed to unmodified antisense strand and applied to HeLa cells grown to 70% confluency by PAMAM-mediated transfection as described herein. Cells were incubated in 1 mL transfection mixture containing 40 .mu.g PAMAM, 100 pmole 5'Cy3-SS/AS duplex siRNAs for 6 hours at 37.degree. C. and washed three times with PBS (Invitrogen) to remove the transfection mixture. Cells were fixed in 100% methanol (pre-cooled to -20C) for 10 minutes, air dried and then re-hydrated in PBS. The uptake of siRNA in HeLa cells was monitored by fluorescence microscope using a Cy3 filter. Exemplary data are shown in FIG. 9. Cy3 Fluorescence represents the localization of duplex siRNA (FIGS. 9A, 9D and 9G). **Overlay images of the Cy3 signal (FIGS. 9a, 9d and 9g) with the DIC (FIGS. 9B, 9E and 9H) indicate that PAMAM-mediated delivery can localize siRNA to both cytoplasm and nuclear regions in the cells (FIGS. 9C, 9F and 91).** Much of the Cy3 fluorescence signal was detected in the nuclear region (FIGS. 9C and 9F) indicating that Lipofectamine.TM. and PAMAM-mediated delivery may have different routings. **[emphasis added].**

Thus, one would have a reasonable expectation of success at making a delivery mixture comprising a dendrimer and a siRNA wherein the siRNA would be capable of mediating RNAi given Szoka et al. teach the dendrimer mixture is capable of delivering nucleic acids into the cytoplasm.

Applicants further argue that Yoo et al., Marcusson et al. and Hu et al. teach cationic lipids deliver the antisense oligonucleotide to the nucleus. None of the cited

references demonstrate the dendrimers were not capable of delivering the oligonucleotide to the cytoplasm, which is only required by the claimed invention.

Applicant's state the present invention provides unexpected results because concentrations above 40 ug/ml are less effective in producing cell uptake and RNAi and none of the cited references, including Yoo et al., alone or in combination indicates an increase in effect with increasing concentration of dendrimer. It must be pointed out that the Yoo et al. references in not cited in the current rejection of record. In response to Applicant's argument, Szoka et al. teach testing various dendrimer to oligonucleotide ratios to determine the optimal amount to use for efficient delivery to cellular compartments (see Table 4). Szoka et al. do specifically teach an oligonucleotide to dendrimer concentration at a ratio of between about 10 ug to 1 mg or 20 ug to 40 ug or about 40 ug, but do teach various ratios of oligonucleotide to dendrimer ratio therefore demonstrating the routine nature of testing various ratios for optimization of the most efficient ratio for delivery and gene inhibition. Therefore because the use of dendrimers in a delivery mixture, as claimed by the instant invention, were known to add benefits to delivery of oligonucleotides molecules to cells, one would have been motivated to make a delivery mixture comprising siRNA and test various ranges for the optimal concentration.

Applicant notes the failure of others is a secondary consideration of nonobviousness and cites Kang et al. and the failure of Bielinska et al. (of record in IDS filed 11/25/2005) to demonstrate that antisense delivery using a generation 5 dendrimer supports a lack of reasonable expectation of success. In response, the claims are not

limited to a generation 5 dendrimer only and Bielinkska is silent with respect to generations 2 to 4 dendrimers and therefore do not provide support for Applicant's arguments. Szoka et al. teach DNA, RNA and RNA:DNA hybrid oligonucleotide molecules wherein the molecules are mixed with PAMAM dendrimers having generations 2 to 5 and therefore one would have been motivated to use any of the dendrimers to find the optimal one capable of efficiently delivering a nucleic acid capable of mediating RNAi. With respect the Kang et al. reference cited by Applicant, this reference was published 3 years after the claimed invention and provide no basis for motivation or the lack of motivation to make a delivery agent comprising a dendrimer and a nucleic acid capable of mediating RNAi. At the time of the instant invention siRNA molecules were known to be more potent and sequence specific for inhibiting gene expression and because siRNAs are inhibitory nucleic acid molecules, one would expect to encounter similar issues in delivery to cells as with the previously known oligonucleotides and therefore one would be motivated to use a delivery mixture comprising a dendrimer because the goal for RNAi is optimal delivery of the siRNA and enhanced cellular uptake by the cells. The use of dendrimers to increase the efficiency of delivery of nucleic acid molecules and one of ordinary skill in the art would have wanted to pursue the known options of increasing the efficiency of nucleic acid molecules that were capable of mediating RNAi.

Thus the rejection of record is maintained.

The rejection of claims 14, 20-28, 30 and 33-44 under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (Clinical Cancer Research 2001 of record cited on PTO Form 892 filed 02/26/2008), Tuschl et al. (cited on PTO Form 892 filed 08/23/05) and McManus et al. (cited on PTO Form 892 filed 08/23/05) Olejnik et al. (cited on PTO Form 892 filed 08/23/05) and Grigoriev et al. (cited on PTO Form 892 filed 08/23/05) and evidenced by Milhem et al. (International Journal of Pharmaceutics 2000, Vol. 197: 239-241 of record cited on PTO Form 892 filed 02/26/2008) is maintained for the reasons of record. The rejection of record is withdrawn for claim 19.

New claims 45-54 are drawn to the same invention as previous rejected and would have been rejected in the rejection of record and thus the rejection above is maintained for claims 45-54. Response to Applicant's arguments will be addressed with the respect to the new claims.

Applicant's arguments in the response filed 10/01/2009 are acknowledged but not found persuasive. Applicant argues that Sato et al. do not provide evidence of delivery of oligonucleotides to confer antisense activity and cite page 3611 third full paragraph as evidence in support of this argument. Applicant has only cited part of the paragraph which states the of distribution of the dendrimer oligonucleotide delivered i.p. to tumor cells. A full reading of the conclusion section does in fact state that G4 complexes show effective delivery to i.p. disseminated tumors and have great potential as delivery vehicles. Thus Sato et al. has shown very specifically that a generation 4 dendrimer can help to overcome some of the disadvantages of delivering nucleic acids to cells, therefore a person of ordinary skill in the art would have good reason to use

such a delivery agent to deliver nucleic acid, such as siRNA, effective to mediate RNAi and would have expected to be able to deliver the nucleic acids to cells and tissues.

As stated previously the examiners reliance on Milhem et al. was only evidentiary for the use of G4 PAMAM dendrimers as efficient drug delivery vehicles and Milhem et al. was not used to teach any of the claimed limitations, such as delivery of a nucleic acid effective to mediate RNAi.

Thus, the rejection of record is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Tracy Vivlemore at 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Kimberly Chong/
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